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| 09/644,668 | 08/24/2000 | Alan J. Korman | 014643-010510US | 5400 |
| 7278 | 7590 | 06/14/2004 | EXAMINER | |
| DARBY & DARBY P.C. P. O. BOX 5257 NEW YORK, NY 10150-5257 | | | OUSPENSKI, ILIA I | |
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1644

DATE MAILED: 06/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/644,668

Applicant(s)

KORMAN ET AL.

Examiner

ILIA OUSPENSKI

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11/26/2003, 01/05/2004, and 03/23/2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 115 - 124, 127, 130 - 133, and 148 - 152 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 115 - 124, 127, 130, 131, and 133 is/are allowed.
- 6) ☐ Claim(s) 148 - 152 is/are rejected.
- 7) ☒ Claim(s) 132 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

RESPONSE TO APPLICANT'S AMENDMENT

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Ilia Ouspenski, Group Art Unit 1644, Technology Center 1600.

2. Applicant's amendments, filed 11/26/2003, 01/05/2004, and 03/23/2004, are acknowledged and has been entered.

Claims 69 – 90, 125 – 126, 128 – 129, and 134 - 146 have been cancelled.

Claims 1 – 68, 91 – 114, and 147 have been cancelled previously.

Claims 115 – 120 and 127 have been amended.

Claims 148 – 152 have been added.

Claims 115 – 124, 127, 130 – 133, and 148 – 152 are pending.

Claims 115 – 124, 127, 130 – 133, and 148 – 152 are under consideration in the instant application.

3. This Office Action will be in response to applicant's arguments, filed 11/26/2003, 01/05/2004 and 03/23/2004.

The rejections of record can be found in the previous Office Actions.

It is noted that New Grounds of Rejection are set forth herein.

The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

4. The Claim for Domestic Priority under 35 USC 119(e): Applicant's remarks pointing out support for the pending claims in the provisional application (60/150,452) are acknowledged, and claims 115 – 124, 127, 130 – 133, 151 and 152 are accorded the benefit of the filing date of the provisional application, i.e. 08/24/1999.

However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 148 - 150 of this application. In particular, it is noted that although there is support for the genus of human antibodies to human CTLA- 4, the Examiner was unable to identify support for an antibody inhibits binding of both B7-1 and B7-1 and competes for binding to CTLA-4 with an 11E8 antibody.

The effective filing date of claims 148 - 150 is therefore considered to be that of the instant application, i.e., 8/24/2000.

5. Prior Objections to the Specification: Applicant's amendments to the Title, Abstract, and page five of the Specification have obviated the objections of record.

6. Prior Objections to the Pending Claims: Applicant's amendments to the Pending Claims have obviated the objections of record.

7. Prior Written Description Rejection of claims 69 – 95, 125 – 129, and 134 – 147 under 35 USC first paragraph: Applicant's cancellation of claims 91 – 95 and 147 has rendered moot the rejection of these claims. Applicant's remarks pointing out written support in the specification for the limitations of claims 69 – 90, 125 – 129, and 134 – 146 have obviated the previous rejection of these claims under 35 USC first paragraph.

8. Prior Rejection of Claims 69 – 74, 77, 80 – 85, 88, 91 – 95, and 147 under 35 USC 102(a) as being anticipated by Hanson et al; claims 91 – 92 and 94 – 95 under USC 35 102(e) or in the alternative under USC 102(a) as being anticipated by Allison et al, as evidenced by Surani et al; and claims 91 – 95 and 147 under 35 USC 103(a) as being unpatentable over Allison et al in view of Kucherlapati et al: Applicant's cancellation of these claims has rendered the rejections moot.

9. Claim 132 is objected to because of the following informality: in the recitation of “affinity of about 10^9 M⁻¹” the molar designation should be in superscript. Appropriate correction is required.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 127, 151, and 152 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein. This is a *New Matter rejection* for the following reasons:

Claims 127 and 151 and dependent claim 152 recite the limitation “does not cross-react with non-lymphoid tissue”. There does not appear to adequate written support describing a subgenus of the human anti-CTLA4 antibodies that do not cross-react with non-lymphoid tissue.

Applicant’s arguments that the genus of antibodies which do not cross-react with non-lymphoid tissues (page 16 paragraphs 1 – 3 of Remarks filed 11/26/2003) can be adequately supported by one species (10D1 antibody), in view of the skill and knowledge in the art, have been fully considered, but have not been found convincing. The rejection is maintained essentially for the reasons of record.

As discussed in the previous Office Action, the instant claims recite the limitation “does not cross-react with non-lymphoid tissue”. There does not appear to adequate written support describing a subgenus of the human anti-CTLA4 antibodies that do not cross-react with non-lymphoid tissue. While Table 4 on pages 80-81 does provide evidence that the 10D1 antibody does not cross-react with non-lymphoid tissue, this description of a single species of 10D1 does not appear to be sufficient to describe the subgenus, as set forth above.

However, it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Thus the specification does not appear to provide an adequate written description of antibodies which “do not cross-react with non-lymphoid tissue.” The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the New Matter in the response to this Office Action.

Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

12. Claims 148 – 150 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein. This is a *New Matter rejection* for the following reasons:

Applicant's amendment asserts that no New Matter has been added. However, the specification does not appear to provide an adequate written description of at least one limitation found in each of independent claim 148. The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Independent claim 148 and claims dependent thereon recite a limitation of a "binding affinity that is about 10^8 M^{-1} or greater." The specification discloses antibodies with an equilibrium association constant of at least 10^8 M^{-1} (e.g. page 5 lines 25 – 28). The recitation of the term "about" would include affinities that are either lower or higher than 10^8 M^{-1} within the scope of the claim, whereas written support is provided only for affinities that are higher than 10^8 M^{-1} .

Thus the specification does not appear to provide an adequate written description of "binding affinity that is about 10^8 M^{-1} or greater." The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

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Applicant is required to cancel the New Matter in the response to this Office Action.

Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

13. Claims 148 - 150 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the antibody designated 11E8 (claim 148) is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the pertinent materials. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, Applicant is required to assure that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications (see 37 CFR 1.808 (a)(2) and MPEP 2410-2410.01).

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 148 and 151 are rejected under 35 U.S.C. 102(e) as being anticipated by Hanson et al (US 6,682,736; see entire document).

Hanson et al teach an isolated human monoclonal antibody or antigen-binding portion thereof that specifically binds to human CTLA-4 with a binding affinity of about 10^{-9} M, and inhibits binding between CTLA-4 and B7-1 and between CTLA-4 and B7-2 (claim 4, column 181 lines 5 – 13; and column 12, lines 42 – 44). Further, Hanson et al teach that their claimed antibodies possess qualities that make them “more efficacious than current therapeutic antibodies against CTLA-4” (column 31 lines 36 – 40).

Since the antibody of Hanson et al inhibits binding of CTLA-4 with B7-1 and B7-2, as do both the antibody of claim 148 and antibody 11E8 of the instant claimed invention, inherent in the teachings of Hanson et al is an antibody which would compete with 11E8 for binding with CTLA-4. Further, since the claimed antibodies of Hanson et al are specific to CTLA-4, and in view of the fact that the expression of CTLA-4 is limited to lymphoid tissue, it follows that the claimed antibodies of Hanson et al anticipate the instant claimed limitation of claim 151 of not cross-reacting with non-lymphoid tissue.

Conclusion

16. Claims 115 – 124, 127, 130, 131, and 133 appear to be allowable.

Claim 132 is objected to for informalities, but would otherwise appear to be drawn to allowable subject matter.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI

Patent Examiner

Art Unit 1644

June 8, 2004

Phillip Gambel
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6/8/04